

## **Explanation of characteristics**

### **characteristics: Sex**

indicates whether the sample came from a female or male human subject.

### **characteristics: Age**

Chronological age at the time of the DNA sample collection.

### **characteristics: Ethnicity**

indicates the racial or ethnic group. Here we use Tsimane Indians (from lowland Bolivia), Hispanics living in the USA, and Caucasian (non-hispanic whites) from the USA.

### **characteristics: DNAmAge**

DNA methylation age, i.e. the predicted age based on the epigenetic clock software (<https://dnamage.genetics.ucla.edu/>) described in the following reference

Horvath S (2013) DNA methylation age of human tissues and cell types Genome Biology PMID: 24138928 .

### **characteristics: AgeAccelerationResidual**

Based on a linear regression line, we defined the measure of epigenetic age acceleration as the difference between the observed DNAm age value and the value predicted by a linear regression model across all subjects. We did not use this measure in our article. Rather, we focused on the following 3 measures.

### **characteristics: AgeAccelerationVSControl**

Based on a natural spline regression line (with 3 degrees of freedom), we defined a "universal" measure of epigenetic age acceleration as the difference between the observed DNAm age value and the value predicted by a spline regression model in control samples. The term "universal" refers to the fact that this measure can be defined in a vast majority of tissues and cell types (with the notable exception of sperm).

### **characteristics: IEAA**

This variable measures the intrinsic epigenetic age acceleration (IEAA) in blood. IEAA measures "pure" epigenetic aging effects that are not confounded by differences in blood cell counts. Our measure of IEAA is defined as the residual resulting from a multivariate regression model of DNAm age on chronological age and various blood immune cell counts (naive CD8 T cells, exhausted CD8 T cells, plasma B cells, CD4 T cells, natural killer cells, monocytes, and granulocytes) which are imputed as described below.

### **characteristics: BioAge4**

This is the biological age measure (number 4) which was constructed in two steps. First, we calculated the epigenetic age measure from Hannum et al (2013, PMID: 23177740) , which measures both intrinsic aging effects and the age related decline of certain blood cell types. Second, we increased the contribution of blood cell types to the age estimate by forming a weighted average of the Hannum predictor with 3 cell types that are known to change with age: naive (CD45RA+CCR7+) cytotoxic T cells, exhausted (CD28-CD45RA-) cytotoxic T cells, and plasma B cells

#### characteristics: EEAA

Quantitative variables that measures the *extrinsic* epigenetic age acceleration (EEAA) which measures epigenetic aging in immune related components.

We defined EEAA in three steps. First, we calculated the epigenetic age measure from Hannum et al (2013), which measures both intrinsic aging effects and the age related decline of certain blood cell types. Second, we increased the contribution of blood cell types to the age estimate by forming a weighted average of the Hannum predictor with 3 cell types that are known to change with age: naïve (CD45RA+CCR7+) cytotoxic T cells, exhausted (CD28-CD45RA-) cytotoxic T cells, and plasma B cells. The resulting measure of blood age is referred to as BioAge4 in our epigenetic clock software (previously defined). Third, we defined a measure of age acceleration (EEAA) as the residual resulting from a univariate model regressing BioAge4 on chronological age. By definition, our measure of EEAA has a positive correlation with the amount of exhausted CD8 T cells and plasmablast cells and a negative correlation with the amount of naïve CD8+ T cells. We note that, by definition, none of our measures of epigenetic age acceleration are associated with the chronological age of the subject at time of blood draw.

#### characteristics: PlasmaBlast

Imputed abundance measure of plasma blasts (activated B cells in blood) based on DNA methylation levels. This ordinal measure has no units. The advanced analysis option of the epigenetic clock software was used to estimate it based on DNA methylation levels.

See the following references

- 1) Horvath S, Levine AJ (2015) HIV-1 infection accelerates age according to the epigenetic clock. J Infectious Diseases; doi: 10.1093/infdis/jiv277 PMID: 25969563
- 2) Horvath S (2013) DNA methylation age of human tissues and cell types Genome Biology PMID: 24138928 .

#### characteristics: CD8pCD28nCD45RA<sub>n</sub>

Imputed abundance measure of exhausted cytotoxic T cells (defined as CD8+, CD28-, and CD45RA- T cells) based on DNA methylation levels. This ordinal measure has no units. The advanced analysis option of the epigenetic clock software was used to estimate it based on DNA methylation levels.

See the following references

- 1) Horvath S, Levine AJ (2015) HIV-1 infection accelerates age according to the epigenetic clock. J Infectious Diseases; doi: 10.1093/infdis/jiv277 PMID: 25969563
- 2) Horvath S (2013) DNA methylation age of human tissues and cell types Genome Biology PMID: 24138928 .

#### characteristics: CD8.naive

Imputed abundance measure of naïve cytotoxic T cells (defined as CD45RA+CCR7+ CD8+) based on DNA methylation levels. This ordinal measure has no units. The advanced analysis option of the epigenetic clock software was used to estimate it based on DNA methylation levels.

See the following references

- 1) Horvath S, Levine AJ (2015) HIV-1 infection accelerates age according to the epigenetic clock. J Infectious Diseases; doi: 10.1093/infdis/jiv277 PMID: 25969563

- 2) Horvath S (2013) DNA methylation age of human tissues and cell types Genome Biology PMID: 24138928 .

characteristics: CD4.naïve

Imputed abundance measure of naïve helper T cells (CD28-CD45RA-CD4+) based on DNA methylation levels. This ordinal measure has no units. The advanced analysis option of the epigenetic clock software was used to estimate it from DNA methylation levels.

See the following references

- 1) Horvath S, Levine AJ (2015) HIV-1 infection accelerates age according to the epigenetic clock. J Infectious Diseases; doi: 10.1093/infdis/jiv277 PMID: 25969563
- 2) Horvath S (2013) DNA methylation age of human tissues and cell types Genome Biology PMID: 24138928 .

characteristics: CD8 T cell

Proportion of CD8+ T cells estimated on the basis of DNA methylation levels with the Houseman algorithm (Houseman 2012, BMC Bioinformatics, PMID: 22568884).

characteristics: CD4 T cell

Proportion of CD4+ T cells estimated on the basis of DNA methylation levels with the Houseman algorithm (Houseman 2012, BMC Bioinformatics, PMID: 22568884).

characteristics: Natural Killer Cell

Proportion of natural killer cells estimated on the basis of DNA methylation levels with the Houseman algorithm (Houseman 2012, BMC Bioinformatics, PMID: 22568884).

characteristics: B cell

Proportion of B cells estimated on the basis of DNA methylation levels with the Houseman algorithm (Houseman 2012, BMC Bioinformatics, PMID: 22568884).

characteristics: Monocyte

Proportion of monocytes estimated on the basis of DNA methylation levels with the Houseman algorithm (Houseman 2012, BMC Bioinformatics, PMID: 22568884).

characteristics: Granulocyte

Proportion of granulocytes estimated on the basis of DNA methylation levels with the Houseman algorithm (Houseman 2012, BMC Bioinformatics, PMID: 22568884).

characteristics: DiseaseStatus

Indicates the disease status: Parkinson's disease or control subject.

characteristics: LevodopaStatus

Medication status with respect to Levodopa medication.

characteristics: LevodopaPerDayIncludingAgonists

Measures the amount of Levodopa medication (including agonists): milligram per day.

characteristics: NumberOfYearsInSchool

Education level= number of years spent in school.

characteristics: SmokingStatus

Smoking status (former, never, current).

characteristics: PackyearsTotal

Total pack years smoking.

characteristics: FamilyHistoryOfParkinsons

Family history of disease.